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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
		ROBERTS	

EXAMINER	

ART UNIT	PAPER NUMBER
	8

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/273,164	Applicant(s) ROBERTS ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14, 30-35, and 51-181* is/are pending in the application.

4a) Of the above claim(s) *35, and 51-181* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 30-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-14, 30-35, and 51-181* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' election with out traverse of Group A (claims 1-14 and 30-34) in Paper #7, filed 9/25/00 is acknowledged.

2. The Restriction Requirement is deemed proper and is therefore made **FINAL.**

3. Currently, claims 1-14, 30-35, and 51-181 are subject to Restriction and Election Requirement. Claims 35 and 51-181 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as claims drawn to a non-elected invention. Group A – Claims 1-14 and 30-34 are pending and under examination.

Drawings

4. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant in parent form PTO-1449, cited the references they have not been considered. (For example see pages 71–75).

6. The information disclosure statement filed 10/1/99 fails to comply with 37 CFR 1.98(a)(3) because document no. B1 PCT 99/06038 does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. Only the English abstract for PCT 99/06038 has been considered, the full reference has been placed in the application file, but the information referred to therein was not considered.

Specification

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. The use of the trademarks has been noted in this application. (.i.e. PCR™ on page 58, FastTrack™ on page 68,etc..). They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Please correct as necessary.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-14 and 30-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 2, 10, and 11 are vague and indefinite in the use of the acronyms PAG2, BoPAG2, PAG4, PAG5, PAG6, PAG7, PAG9, BoPAG2, BoPAG4, BoPAG5, etc. The terms should be defined in their first instance. It is not clear if applicant intends to claim any prior art structures employing the same acronyms or specific sequence identification numbers. For example, BoPAG2 refers to Seq. Id. No:25 identified in the specification on page 8, line 19-21. In order to further clarify the claims it is suggested that the seq. Id. numbers be incorporated into the claims. This initial explanation will convey intended meaning with subsequent abbreviations. Please identify applicants intended meaning.

B. Claim 9 is vague and indefinite in the use of the phrase "immunologic detection". Although the term is briefly cited in the disclosure (page 6, lines 6-16), the definition is not given. The recitation of known methods without an explanation of what the phase "immunologic detection" entails is not clear. Since the term is not defined in the disclosure, the metes and bounds of the claim can not be determined. It is suggested that applicant define the term or list suitable methods in the claim.

C. Claims 10 and 11 recites the limitation "polyclonal antisera" and "monoclonal antibody preparation" respectively. The wording is vague and indefinite because it is not known if applicants are claiming antibodies or if the claims include for

example materials made from/involved in antibody production. Are the PAGs reacted with antibodies or another composition? Please explain.

D. Claims 1-14 and 30-34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below:

The claims are drawn to an assay method that employs antibodies. The antibodies bind with an pregnancy associated antigen to form an antibody-antigen complex which is detectable and indicative of pregnancy in the animal, but the method does not indicate that a complex will be formed or identified. The recitation of a method step requires at least a contact step, a detection step, and a correlation step. Please include the appropriate steps.

Further, there are no claimed steps reciting the washing or removal of unbound materials. If no separation will be performed it is not clear how the complex will be identified from the reaction solution (unbound material).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1, 3, 5, 6, 9, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Roberts et al. (Aspartic Prot., Struct., Funct., Biol., Biom., Impl., 231-240, 1995).

Roberts et al. evaluate maternal serum concentrations for pregnancy-associated glycoproteins (PAGs) and correlate this measurement to pregnancy in cattle and sheep. (See abstract). The profile of bovine PAG in serum samples from cows revealed that the proteins were expressed just prior to implantation until term (~145 days in sheep, ~280 days in cattle). See page 235.

II. Claims 1, 3, 5-6, 9, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Zoli et al. (Biology of Reproduction, 46, 83-92, 1992).

Zoli et al. disclose a double antibody radioimmunoassay for a bovine pregnancy-associated glycoprotein (bPAG). The RIA allowed for PAG measurement in placental extracts, fetal serum, fetal fluids, serum, or plasma samples from pregnant cows. Peripheral serum bPAG levels increased progressively throughout the pregnancy. bPAG levels peaked at days 1-5 prior to parturition and was undetectable at day 100 +/- 20 after parturition.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 4, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (Aspartic Prot., Struct., Funct., Biol., Biom., Impl., 231-240, 1995) or Zoli et al. (Biology of Reproduction, 46, 83-92, 1992) in view of Sasser et al. (J. Reprod. Fret., Suppl. 37, 1989, 109-113).

Please see discussion of Roberts et al. and Zoli et al. as set forth above.

Roberts et al. and Zoli et al. differ from the instant invention in failing to specifically teach saliva, milk, or urine as samples to evaluate PAG concentrations.

Sasser et al. disclose a radioimmunoassay to detect PAG (also known as PSPB). The samples under investigation included body fluids other than blood, particularly milk, urine, tears, saliva, vaginal secretions, and cervical secretions. PSPB (Applicants PAG) levels were detected in milk at times when PSPB was excessively high in the plasma of cows. Although PSPB was not found to specifically react with the antigens used by these investigators in urine, tears, saliva, vaginal secretions, and cervical secretions these mediums were taught as possible samples to evaluate PSPB.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the various known samples (milk, urine, tears, saliva, vaginal

secretions, or cervical secretions) taught by Sasser et al. in the method of either Roberts et al. or Zoli et al. to detect pregnancy in a bovine animal, because such samples as taught by Sasser et al. are well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing any of the known sample mediums, because these samples were previously considered likely sources for PSPB an indicator of in pregnancy testing for livestock. (page 110, 2nd paragraph, Biological Characteristics).

One having ordinary skill in the art would have been motivated to detect PSPB levels in any of these disclosed samples in order to detection bovine pregnancy, because such body fluids were known. Given the diversity of PSPB and its expression (having various possible antigen reactivity), it would have been advantageous to measure different samples for possible PSPB concentrations and relate those measurements to pregnancy.

II. Claims 2, 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (Aspartic Prot., Struct., Funct., Biol., Biom., Impl., 231-240, 1995) or Zoli et al. (Biology of Reproduction, 46, 83-92, 1992) in view of Xie et al. (Proc. Natl. Acad. Sci. USA, Vol.94, 12809-12816, 11/1997).

Please see discussion of Roberts et al. and Zoli et al. as set forth above.

Roberts et al. and Zoli et al. differ from the instant invention in failing to specifically teach the different types of bPAGs having possible utility in bovine pregnancy detection.

However, methods of producing varying PAG structures, which are measurable indicators of bovine pregnancy, were previously taught in the art. Specifically, Xie et al. disclosed "that cattle possess many, possibly 100 or more, PAG genes, many of which are placentally expressed". (Abstract) These PAGs are also known as pregnancy-specific protein B (12809, 2nd column, 2nd paragraph). Bovine (boPAG) were cloned and screened with mixed probe containing PAG1 and PAG2. A second screen was conducted to identify boPAG transcripts that reacted with anti-boPAG1 antiserum. (page 12810 – Materials and Methods) Fig 8 outlines all of the known cloned PAGs.

Roberts et al. or Zoli et al. in view of Xie et al. are all analogous art because they are from the same field of endeavor, all three inventions teach PAG detection procedures.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the various known PAG bovine clones as taught by Xie et al. in the method of either Roberts et al. or Zoli et al. to detect pregnancy in a bovine animal, because such PAGs as taught by Xie et al. are well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing any of the known bovine PAGs, because these compounds were previously associated in pregnancy testing for livestock. (page 12809, 2nd column, 2nd paragraph).

One having ordinary skill in the art would have been motivated to detect varying PAGs in bovine pregnancy detection and evaluation because the PAGS were taught to be highly diverse in sequence with considerable functional multiplicity. (See abstract)

III. Claims 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (Aspartic Prot., Struct., Funct., Biol., Biom., Impl., 231-240, 1995) or Zoli et al. (Biology of Reproduction, 46, 83-92, 1992) in view of Xie et al. (Biology of Reproduction 57, 1384-1393, 1997) and in further view of Gerrie et al. (Clinica Chimica Acta, 155, 1986, page 51-60).

The teachings of Roberts et al. or Zoli et al. in view of Xie et al. are set forth above.

Although these references do not specifically state that a double antibody -ELISA procedure in employed to detect PAGs in a bovine sample, it is well known to those with ordinary skill in the art that ELISA assays are commonly used for such a purpose. Methods for determining this data can be achieved by procedures known to those of ordinary skill in the art.

Gerrie et al. teach a sensitive enzyme-linked immunoassay to detected a pregnancy-associated alpha$_2$-glycoprotein. Plates coated with sheep anti-human α_2 – PAG were incubated with the target sample, rabbit anti-human α_2 –PAG, and goat-anti-rabbit IgG peroxidase conjugate. The peroxidase reaction was measured and correlated to PAG concentrations in the sample. (See page 53-54, especially Assay procedure).

It would have been prima facie obvious to one of ordinary skill in the art to determine the amount of pregnancy associated glycoproteins in bovine samples by ELISA as demonstrated by Gerrie et al. in the methods disclosed by Roberts et al. or Zoli et al. in view of Xie et al. with a reasonable expectation of success and little

additional labor because this information can be easily determined utilizing reagents (i.e. antibody compositions) that are already being used in their methods. The ELISA assay procedures employed in the teachings of Gerrie et al. would have been an obvious substitution to the RIA/detection procedures taught by Roberts et al. or Zoli et al. in view of Xie et al. for the detection of pregnancy associated glycoproteins because it is well known to those of ordinary skill in the art at the time of applicant's invention that ELISA produces increased assay sensitivity. This point is seen in the U.S. Patent#4,271,140 – Bunting, which state that double receptors assay improve sensitivity (see abstract and col 2). This patent is merely cited in support of Examiners position with respect to ELISA protocol sensitivity and assay improvement at the time of applicant's invention. It is not intended to be utilized as part of the instant rejection.

One of ordinary skill in the art would utilize various comparative assay formats for the resulting data sets to evaluated PAG concentrations. These procedures/assay formats are routine optimizations that are almost always determined and used in immunoassay studies. Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to employ known assay protocols in the given parameters to determine the unknown as a means of optimizing the assays provided by the art.

11. For reasons aforementioned, no claims are allowed.

Remarks

12. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Scott et al. (Clin. Exp. Immunolo., 1985, 59, 564-570) teach an enzyme-linked immunosorbent assay to detect α_2 –PAG in serum samples during pregnancy.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook

Lisa V. Cook
CM1-7D16
(703) 305-0808
12/14/00

RODNEY P. SWARTZ, PH.D
PRIMARY EXAMINER